Teaming up: from motors to people

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ABSTRACT **When I reflect on how I became a cell biologist and why I love being one today, one thing that comes to mind is the many terrific collaborations I have had. The science I am most proud of from my graduate and postdoctoral training would not have been possible without working in teams with other scientists. Now, in my own group, much of our best work is being done collaboratively, both within the lab and with other labs. In this essay, I will highlight my experiences working in teams as a trainee, the role teamwork has played in my own research group, and how important I think collaborative science is for the future of biological research.**

COLLABORATIONS AS A TRAINEE

One of my earliest experiences with collaboration across disciplinary boundaries happened when I was a graduate student in the Cell Biology Department at Yale University, working with Mark Mooseker and Peter Novick. During the course of my PhD, work from the Cheney, Mooseker, and Spudich labs showed that single molecules of vertebrate myosin Va can take multiple steps along their tracks (Mehta *et al.*, 1999); this was the first known example of a processive myosin motor. I wanted to determine whether this was a general property of this class of myosin, so I focused on characterizing the motile properties of the two yeast class V myosins. To pursue this goal, however, not only did I need the tools of molecular and cellular biology, which I had, but also those of biophysics, which I didn't have. I found that the best way to learn a new field was by working closely with someone who already knew it well. One of the postdocs in the lab, Matt Tyska (now an associate professor at Vanderbilt University), was a biophysicist. Over the course of our collaboration, I learned how to analyze, quantify, and interpret in vitro motility data. Ultimately, we showed that, in contrast to their vertebrate counterparts, the yeast myosin Vs are not processive motors (Reck-Peterson *et al.*, 2001). Exciting work from the Trybus lab later showed that efficient transport in cells likely requires the recruitment of motor teams onto cargo (Sladewski *et al.*, 2013) or track modifications (Hodges *et al.*, 2012), which can convert the nonprocessive yeast myosins into processive motor-cargo complexes.

In addition to learning some biophysics from Matt, I learned the importance of asking questions and saying, "I don't understand," especially in the context of work outside my scientific comfort zone. Asking "naive" questions offers an opportunity to re-examine fundamental assumptions in a field. On the other hand, working across disciplines means we must rely on our colleagues' expertise, and they on ours, so teaching each other the standards of proof and intellectual rigor of our respective fields becomes essential. As with molecular motors, teams of people with different backgrounds have unique emergent properties that can drive discovery.

While working on the biophysics of myosin V, I realized that I wanted to learn more about how molecular machines work, so I continued to pursue my fascination with molecular motors in the lab of Ron Vale at the University of California, San Francisco. As a postdoc, I turned my focus to the microtubule-based motor cytoplasmic dynein, which at the time was (and arguably still is) the least understood of all the cytoskeletal motors. Once again, collaboration was essential for progress. To determine how dynein worked, we first needed to figure out how to make the protein recombinantly, purify it, and develop and implement assays to study its motile properties. Dynein is a particularly challenging protein because of its large size: the holoenzyme has a molecular mass of ~1.5 MDa. Together with Andrew Carter (now a group leader at the MRC Laboratory of Molecular Biology), I devised methods to purify and express recombinant dynein in *Saccharomyces cerevisiae*. Later, Ahmet Yildiz (now an assistant professor at the University of California, Berkeley) and Arne Gennerich (now an assistant professor at the Albert Einstein College of Medicine) joined the project. All four of us were involved in developing assays to study dynein's single-molecule motility

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Abbreviations used: BWF, Burroughs Wellcome Fund; HHMI, Howard Hughes Medical Institute; PI, principal investigator.

behavior, with Ahmet and Arne focusing on analyzing dynein's stepping behavior and response to force with high precision. As a group, we discovered that single dynein molecules are processive motors that step more variably than other motors (Reck-Peterson *et al.*, 2006) and that dynein also displays unique force-dependent stepping behavior (Gennerich *et al.*, 2007).

There is nothing more exciting in science than being in the midst of discovery; the intense daily conversations I had with Andrew, Arne, and Ahmet about how dynein might work dramatically fueled our progress. I remember this as one of the most rewarding times of my scientific career. We all brought different skill sets to the team, which allowed us as a group to do what we could not have done alone. However, our close collaboration also posed its own challenges. I found that working closely with peers can create competition, insecurity, and anxiety about recognition. Nonetheless, despite some of the difficulties of working together on a highly competitive project, Andrew, Ahmet, Arne, and I became and remain good friends, and we all left the Vale lab with jobs that would allow us to pursue the science we loved.

COLLABORATIONS AS A PRINCIPAL INVESTIGATOR

When I started my lab at Harvard Medical School in 2007, I knew that I wanted to study intracellular transport ranging from the biophysical properties of the motors to the cell biological functions that require motor activity. As I had learned from Ron's example, this would require an interdisciplinary team that included people with skills in single-molecule biophysics, genetics, biochemistry, and live-cell imaging. Therefore I recruited both physicists and biologists to the lab. One of the great things about pairing physicists and biologists is that they tend to approach problems from different viewpoints. The physicists tend to first ask "How does it work?," while the biologists' first question is often more along the lines of "Why does it matter?" This cultural tension is exciting, because it helps us define problems we might not have recognized working as individuals.

We decided to tackle some big problems. We wanted to understand how dynein steps processively (Qiu *et al.*, 2012), how it is regulated by some of its essential cofactors (Egan *et al.*, 2012; Huang *et al.*, 2012), how teams of motors work together (Derr *et al.*, 2012), and what the structural basis for dynein's interaction with microtubules is (Redwine *et al.*, 2012). Four of the papers that we published addressing these problems had co–first authors. All four projects also involved collaborations with other colleagues of mine at Harvard. We integrated DNA nanotechnology approaches into our studies by working closely with William Shih (Derr *et al.*, 2012; Qiu *et al.*, 2012) and structural electron microscopy by working with Andres Leschziner (Huang *et al.*, 2012; Redwine *et al.*, 2012). While a great deal of work remains before we can fully answer these four questions, I know that the discoveries we have made so far required teamwork and that our discoveries of the future will too.

Working collaboratively might be vital to success, but that doesn't make it easy. Just as I had suffered from feelings of competition, insecurity, and worry about recognition, I saw that my students and postdocs had some of these same feelings and concerns. To

FIGURE 1: Motors and martinis: the Reck-Peterson lab building teamwork skills at a cocktail party. Seated (left to right): W. Qiu, S. Reck-Peterson, J. Huang, K. Tan, S. Zou, and A. Roberts. Standing (left to right): W. B. Redwine, M. Cianfrocco, M. Egan, M. McClintock, and B. Goodman.

foster a culture of teamwork, I invested time in talking to my lab members about the human component of their collaborations. I listened to them and took their concerns seriously. Like any partnership, collaborations in science sometimes require an investment in making the relationship work (Figure 1). Things haven't always been perfect, but I think we would all say that together we built a strong lab culture that values and respects teamwork. In fact, well before we had published any papers from the lab, I knew that things were on the right track when one of my graduate students came to my office and asked me, "Can I have a collaborator too?"

THE IMPORTANCE OF TEAMWORK FOR THE FUTURE OF THE BIOLOGICAL SCIENCES

While doing science collaboratively is not for everyone, I think teamwork is essential in the modern biomedical research arena. Increasingly, the types of problems that we tackle require more interdisciplinary approaches and larger numbers of people than in the past. Particularly in the culture of the United States, which prizes the individual, it will be challenging to change the ways in which we acknowledge and reward discoveries so that teamwork is appreciated. We need to recognize starred first and cocorresponding authorships as truly equal contributions (which is not always the case), and this recognition should be reflected in how we make decisions about hiring, promotions, and funding allocation. The multiple program director/principal investigator model adopted by the National Institutes of Health in 2006 was an important step toward realizing these goals.

We also need to invest in training principal investigators (PIs) how to manage teams. A decade ago, the Burroughs Wellcome Fund (BWF) and the Howard Hughes Medical Institute (HHMI) recognized the need for this type of training and developed a course, which I took, and published a book on lab management (BWF/HHMI, 2006). I've also taken a course run by hfp consulting (www.hfp-consulting.de), a firm specializing in teaching leadership and management skills to scientists. From these experiences, I learned a few important things about how people and teams work. For example, I learned some of the theory behind group dynamics, which has helped me to recognize how individuals within teams may perceive their roles in different ways and that this can change over the course of a project. Through personality assessment analysis, I've learned to recognize and appreciate different personality types, which has helped me construct teams and manage conflicts as they arise. The management skills of PIs not only affect scientific productivity but also set examples that will influence the next generation of scientists. Therefore it is important that we invest resources, both human and financial, into this type of training and make it accessible to more people.

I was deeply honored to receive the Women in Cell Biology Junior Award, and I am also grateful for the opportunity that the award provided me to reflect on the work that has brought me to this point. So much of my career thus far has critically depended on working with others, both as a trainee and now in my own lab. In the future, I will continue to encourage and facilitate collaborative science within my lab, institution, and field. I also hope to help break down the cultural obstacles we have toward recognizing and rewarding teamwork in the biological sciences.

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